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(54) Title: COMPOSITIONS FOR USE IN DENTISTRY

(57) Abstract

A composition that can be used for tooth restoration comprises a filler in the form of particles capable of space filling to a void volume of less than 20 %, and an activatable binder resin precursor, the composition being mouldable under vibration at a frequency of 50 Hz to 50 kHz.

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COMPOSITIONS FOR USE IN DENTISTRY

This invention relates to compositions for use in dentistry.

Background of the Invention

The restoration of a tooth involves the repair of two structures, the resilient inner dentine core and the hard, stiff enamel shell. Present-day composites are good substitutes for dentine, matching both its strength and stiffness. However, they are too flexible to restore the outer enamel shell. Enamel has a Young's modulus of about 30 GPa; the most stiff posterior composites, even when fully cured, have stiffnesses of less than 15 GPa.

An increase in filler content of the composite, to greater than 85% volume fraction, should increase the stiffness of the composite to a level close to that of enamel. However, the handling properties of such composites in their uncured state are different due to their tendency to fragment under the slightest shear.

GB-A-2115799, GB-A-2075035, GB-A-1591741, GB-A-2173206, US-A-4381918 and US-A-4540723 disclose dental materials comprising inorganic filler, monomer, polymerisation promoter and curing agent. GB-A-2115799 additionally discloses the use of a solvent, for the purpose of dissolving silicon alkoxide and organic metal compound.

US-A-4392828 discloses a method of producing a dental restorative which involves heating the composite, e.g. with vibration, in order to fuse glass fibres.

Summary of the Invention

According to the present invention, a composition comprises a filler in the form of particles capable of space filling to a void volume of less than 20% and an activatable binder resin precursor; the composition is mouldable under vibration at a frequency of 50 Hz to 50 kHz, and can be so used in dentistry. The composition can be formed, without heating, by mixing the components with the volatile diluent, e.g. with vibration, and removing the

diluent. The invention provides a method of placement and manufacture of composites having at least 85% filler loading, and as high as 95% volume fraction if combined with established computer particle size mixing techniques.

Detailed Description of the Invention

In preparing a composition of the invention, the chosen filler is first mixed to achieve a particle size distribution capable of space filling to a void volume of less than 20%. The filler is preferably silane-coated, e.g. by proprietary methods, dried, then mixed with the premixed binder resin containing both active monomers and a demand curing system and a volatile diluent that is not a radical inhibitor. The viscosity of the resulting mixture is controlled by the volume of inactive volatile diluent. Any volatile organic liquid can be used, e.g. ethanol (absolute alcohol is preferred), acetone, ether, chloroform, trichloroethane, CFC's, fluorocarbons and isopropyl alcohol.

The volatile diluent allows the setting up of hydrostatic capillary forces between the filler particles, which pull the particles together. Applying ultrasound to the mixture allows the solids to reach a high packing density and low energy state without having to apply too much energy.

Application of the ultrasonic probe for a few minutes is sufficient to complete the process. Further application of ultrasound has no further effect on the material. Too vigorous application of the ultrasound may heat the material, boil off the volatile diluent, and cause cavitation.

The slurry, prior to drying, can be either spread out in a layer to dry or first ultrasonicated, then dried slowly as a plug in the container in which it is ultrasonicated. For example, the mixture is dried into a layer about 1-2 mm thick. At this stage, the volatile diluent is removed by surface evaporation, as boiling off will cause cavitation. This is performed in the dark, e.g.

a black tunnel, if necessary to prevent light activation of the resin precursor.

If the process has been performed correctly, the mixture will now have a closely-packed grain structure. Each "grain" will be composed of many smaller micro particles packed around a larger macro grain, and will be about 200 μm across. The inter-grain boundaries will be filled by residual monomer. Formation of this structure is sensitive to the materials used. The grain structure is a good indication of the process having been carried out successfully.

The dried mixture is a friable cake material. The material should be broken as little as possible, to reduce the ingress of air. Alternatively, the dried mixture should be moved into a vacuum chamber and packed under low pressure.

The lower the binder content, the less waxy the material. When ultrasonicated (vibrated under pressure), a waxy dough is formed that, by further ultrasonication, can be packed, e.g. placed in a well. When the material is pushed into a well, more of the volatile diluent is squeezed out and the material becomes clearer. When viewed under a microscope, the material has undergone a change similar to sintering, creating an amorphous secondary structure.

Further vibration allows the removal of the wax, and/or its manipulation and modelling into precise shapes. Once in position, the waxy solid can be converted to a hard, cured composite by shining a light upon the wax for less than 40 seconds, the exact time for cure varying with the level of light-activatable activator and the composition of the filler particle mix.

The filler content of the final wax solid can be from 65-95% volume fraction. The filler preferably comprises particles of inorganic glass, glass ceramic, metal/inorganic salt or oxide of particle sizes ranging from 0.01 to 100 μm in diameter. The preferred particle

size is 0.05 to 20 μm, e.g. 0.1 to 15 μm, and most preferably no more than 10 or, better, 5 μm. If necessary, suitable material of larger size may be subjected to ball-milling.

The filler may be radio-opaque or radio-translucent. The filler may be coated with vinyl silanes to improve adhesion between the filler and the organic matrix. The particle size distribution of the fillers will be such that the interstitial volume between particles is reduced to a minimum by the filling of such spaces with ever finer particles, to achieve optimal filler loading.

The binder resin can be any form of radically-polymerising monomer. The preferred monomers are acrylates having two acrylic groups per molecule. The molecular weight of such materials rises rapidly during the cure process, to levels at which structurally strong and stiff polymers result. In particular, aromatic dimethacrylates such as BisGMA, based on a Bisphenol A core, are very successful. Lower molecular weight dimethacrylates can be used as viscosity modifiers; allyl methacrylates are also useful in this respect.

The curing systems are preferably of a demand-curing type. Heat curing may involve the use of peroxides or azonitriles and other radical sources activated by heat. Radio frequency and magnetically-induced heat sources can be incorporated into the uncured paste. The paste can be activated by radiation, be it electro-magnetic or ionising, with or without activators. For light activation, α-diketone amine systems can be used for blue light-curing, benzoin methyl ether for ultra-violet cures.

As is well known in the art, a stabiliser/catalyst may also be used. A conventional material of this type is dibutyltin dilaurate, but alternative materials include dimethyl-p-toluidine.

The placement of the highly-filled composite in a well or cavity is performed with the aid of a device capable of vibrating at a frequency between 50 Hz and 50 kHz. In a

preferred embodiment, the device is an ultrasonic probe. Conventional such devices vibrate at 30-42 kHz. Such a probe can thus be used to mix the components, to assist placement of the dried material into wells or other storage means, and also to fill a dental cavity.

The composite can be supplied as a powder in a compule, the vibrating device being used to extrude the powder from the mouth of the compule in the form of a waxy solid. The compule may be designed to allow the extruded bolus of wax to be placed and compacted in the tooth cavity in one action, or a second vibrating device may be used for compaction.

In particular, the material may be placed in contact with a sheet of Perspex or other suitable material having a number of apertures, e.g. wells, and pushed into the wells by vibration with, for example, an ultrasonic probe.

There are advantages, from the quality control point-of-view, to compact the powder to a wax at the factory stage. For example, the wax-like material may be packed, not in compules but as a sheet from which the bolus is picked up on the tip of a compacting vibrator. This tip, having the modification of a retractable cylindrical sheath that cuts a circular plug of wax, holds it to the vibrator tip, and then deposits the wax in the cavity as it is vibrated. The wax sheet should be protected from light during transport and in the surgery during use. A carousel arrangement that exposes only part of the sheet of wax to the vibrator sheath, yet protects the bulk of the wax, provides one solution to the packaging problem.

The carousel may contain the composite in the powder stage, the vibrator compacting and cutting a wax plug in one action. The powder may be placed directly into the cavity, but this is less preferred.

The composite is normally cured in the mouth. However, the wax composite could be compacted into a die or mould outside the mouth. In this way, inlays and onlays can be produced for later cementation. If larger

structures are produced using vibrating extruders, they can be heat-cured into blanks for use in CAD/CAM cutting machines. In this way, devices can be precision-milled, then cemented into place in the tooth cavity. The blanks can be cured by electron beams or induced heat sources, e.g. RF or magnetic.

By way of example, in order to apply the material, a bolus is removed from its carrier/well, e.g. the block from the Perspex carrier, by applying the end of aplastic amalgam carrier (e.g. as available from Premier Dental). The amalgam condenser should be a push fit for the hole in the block. The bolus is wedged into the cavity and is then carved into place by the vibrating tool. Application of vibration will shear the material along the grain boundaries. The material is then light-cured in situ.

The present invention allows the use of high filler levels: the higher the volume filler loading, the lower the setting shrinkage. Setting shrinkage is clinically undesirable because it can cause pain, due to a flexing of the tooth, and increases the probability of marginal leakage.

Further, the higher the filler loading, the higher the proportion of filler on the surface. Hence only small abrasive particles are needed to cause attrition. Therefore the resultant filling wears less in service.

Another advantage of the invention is that, the higher the filler content, the better the match between the Young's moduli of the enamel shell of the tooth and the composite. Therefore there is a better distribution of stresses within the restored tooth.

A further advantage is that the higher stiffness and lower shrinkage of the composition make the filling of large cavities more clinically feasible. The high filler content allows the material to be carved to the required shape in the cavity, without slumping, using a vibrating tool; this is by contrast to existing materials that slump and make carving difficult and time-consuming.

A possible disadvantage of the high filler content can be that the material is abrasive. Particularly with a view to minimising wear on opposing teeth, it is preferred that the filler particles should not be too coarse.

In order to avoid abrasion, all stainless steel surfaces should therefore be coated with a hardened layer. For example, a diamond-like carbon or a titanium nitride coating, ball-mill surfaces, and other exposed manufacturing surfaces, should be coated with a Teflon coating plus silica and replaced during use, e.g. at weekly intervals. These techniques are known in the industry.

The following Examples illustrate the invention.

Example 1

A silanated lead glass (particle size distribution 15-2 μm) is mixed at a ratio of 80:20 with a fumed silica of particle size <0.75 μm. The components are mixed by end-over-end rotation in a sealed vessel.

75 g bis-GMA, 23 g triethylene glycol dimethacrylate, 0.1 g camphorquinone and 0.1 g of dibutyltin dilaurate are mixed well. At a mixing ratio of 1:2, absolute ethanol is added.

0.45 ml of the liquid mixture is added to 1 g of the powder and mixed thoroughly, ultrasonicated for 2 minutes and then allowed to dry for 24 hr in the dark at 30°C. The resulting powder is spread out and dried in the same manner as before for a further 24 hr.

The powder compacts to a wax under gentle pressure from a mechanical amalgam plugger. When exposed to light of wavelength 470 nm for 30 seconds, the wax turns to a hard solid with a compressive strength in excess of 270 MPa.

Example 2

45 g Raysorb T3000 (Esschem; 15 μm in size) and 5 g Silica OX50 (Degussa) are tumbled in a vee mixer for two hours. 1 part by weight of this powder is mixed with an equal weight of absolute alcohol. The resultant slurry is stirred with an ultrasonic probe for two minutes.

A liquid is prepared by mixing 1% dibutyltin dilaurate (Aldrich), 1% camphorquinone (Aldrich), 24% tetraethylene glycol dimethacrylate (Aldrich) and 74% Bis-GMA (Freeman Chemicals). Starting with 0.168 part of the liquid, it is added to the slurry which is stirred until homogeneous, then spread out into a layer about 3 mm thick and placed in a dark tunnel having a glass base. Air is blown through the tunnel until alcohol is undetected in the effluent. The process is initially conducted cool (15°C), warming to <60°C.

The resulting cake has a structure that should be broken as little as possible. The cake is transferred to a packaging station of the type described above, in one piece, then pushed into the Perspex holders using an ultrasonic probe of sufficient diameter to be a push fit into the hole.

The ultrasonic probe can be obtained from Jencons (600W, 20 kHz). The probe should be wide enough to be modified for the packing of prototype blocks.

Example 3

The procedure of Example 2 is repeated, except that the Raysorb component is first ball-milled to <5 μm. When this is done, the fumed silica content must be reduced to match the new particle size profile. This necessitates the reduction of the silica fraction by approximately 50%. Optimising the silica is preferably done using an optical microscope. When the silica content is right, the drying cake can form large hexagonally packed structures.

In use as a dental composite, the cavity where the material is applied should be prepared in the usual way, as for other dental composites.

The hardness, crack-pinning characteristics and Young's modulus of the material are all better than existing composites. The longitudinal shrinkage for the composite of Example 2 was 0.42%, whereas the value for one of the current market leaders (Heliomolar) was 4.0%.

Restrained shrinkage is probably the best approximation of what goes on in the mouth, as the material is usually restrained by the surface of the natural tooth. The values for the novel composite and Heliomolar were respectively 0.38% and 1.3%. Moreover, the Heliomolar had internal cavities, causing points of weakness, formed during restrained shrinkage.

CLAIMS

1. A composition comprising a filler in the form of particles capable of space filling to a void volume of less than 20%; and an activatable binder resin precursor; the composition being mouldable under vibration at a frequency of 50 Hz to 50 kHz.

2. A composition according to claim 1, in which the ratio of filler to resin precursor is 80-97:20-3 v/v.

3. A composition according to claim 1 or claim 2, in which the particles are coated with a silane or other material that promotes adhesion between the filler and the binder resin.

4. A composition according to claim 3, in which the coating material is a vinyl silane.

5. A composition according to any preceding claim, in which the resin precursor comprises a radical-polymerisable monomer and a radical-generating agent.

6. A composition according to claim 5, in which the monomer comprises two acrylic groups per molecule.

7. A composition according to any preceding claim, in which the said void volume is less than 10%.

8. A composition according to claim 7, in which the void volume is less than 5%.

9. A composition according to claim 7, in which the void volume is no more than 3%.

10. A composition according to any preceding claim, which is dry.

11. A composition according to any preceding claim, in which the particles are less than 5 μm in size.

12. A composition according to any preceding claim, for therapeutic dental use.

13. A cured composition as obtained by activating the resin precursor and thereby curing a composition according to any of claims 1 to 12.

14. A device including a container containing a composition according to any of claims 1 to 12, the device or container also including a portion that is movable or

removable to provide an aperture through which the composition can be extruded or dispensed.

15. A device according to claim 14, which additionally comprises means for transferring a bolus of the composition from the container.

16. A device according to claim 15, which additionally comprises means for vibrating the bolus.

17. Use of a filler and a resin, each as defined in any of claims 1 to 6, for the manufacture of a prosthesis for use in dentistry.

18. Use according to claim 17, wherein the filler particles are less than 5 μm in size.

19. A method for preparing a composition according to any of claims 1 to 11, which comprises mixing the filler and the precursor with a volatile diluent, and removing substantially all the diluent, without the application of heat or activation of the precursor.

20. A method according to claim 19, which additionally comprises filling the composition into cavities.

21. A method according to claim 19 or claim 20, wherein the mixing and/or the filling comprise ultrasonication.

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl. 5 A61K6/083

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
Int.Cl. 5	A61K ; A61C

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched[8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category *	Citation of Document,[11] with indication, where appropriate, of the relevant passages[12]	Relevant to Claim No.[13]
Y	GB,A,2 201 093 (G-C SHIKA KOGYO K.K.) 24 August 1988 see page 5, paragraph 2 see page 6, line 12 - line 14	1-21
Y	EP,A,0 091 990 (BLENDAX-WERKE R. SCHNEIDER GMBH & CO) 26 October 1983 see claims	1-21
A	EP,A,0 395 427 (NATIONAL RESEARCH DEVELOPMENT CORPORATION) 31 October 1990 see page 2, line 1 - line 4	
A	BE,A,765 627 (J. VARGA) 30 August 1971	
A	US,A,4 219 619 (M.ZAROW) 26 August 1980	

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* Special categories of cited documents :[10]

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IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
14 APRIL 1992	06. 05. 92
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	G COUSINS-VAN STEEN

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
X,P	DE,A,4 032 505 (THERA PATENT) 14 August 1991 see column 2, line 54 - column 3, line 44; claims	1-21

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. GB 9200103 SA 55563

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 14/04/92
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		JP-A- 2302409	14-12-90
BE-A-765627	30-08-71	None	
US-A-4219619	26-08-80	None	
DE-A-4032505	14-08-91	None	